

AMENDMENT

In the Specification:

Please replace paragraph [0017], beginning on page 6, with the following rewritten paragraph:

[0017] --Particular nucleotide sequences in a nucleic acid often direct the type of secondary structure or structures that the nucleic acid is capable of adopting. For example, nucleic acid sequences conforming to the motif $(G_aX_b)_cG_a$ sometimes form an intramolecular chair G-quadruplex structure. Sometimes a is an integer between 2 and 6 and b is an integer between 1 and 4, and often, b is the integer 2 or 3. In another example, quadruplex-forming nucleic acids sometimes comprises or consists of a nucleotide sequence that conforms to the motif $(GGA)_4$ (SEQ ID NO: 11) or $(GGA)_3GG$ (SEQ ID NO: 18), where G is guanine and A is adenine, which sometimes form structures that comprise a tetrad stabilized by second planar structure in a parallel orientation to the tetrad. The second planar structure includes five or more nucleotides in the nucleic acid and thereby forms a structure that is larger than a tetrad. For example, the second planar structure can contain five, six, seven, eight, nine, or ten nucleotides to form a pentad, hexad, heptad, octad, nonad, or dectad, respectively. A nucleic acid often includes one or more flanking nucleotides on the 5' and/or 3' end of the nucleotide sequence that forms the quadruplex and are not part of the quadruplex structure. These motifs can be used to identify other quadruplex-forming sequences in regions of a genome operably linked to a gene. G-quadruplexes formed by sequences conforming to this motif sometimes include 2 to 6 G-tetrads, and often include between 3 and 5 G-tetrads.--

Please replace paragraph [0019], beginning on page 8, with the following rewritten paragraph:

[0019] --A nucleic acid sometimes includes a nucleotide sequence similar to or substantially identical to a native nucleotide sequence. A similar or substantially identical nucleotide sequence may include modifications to the native sequence, such as substitutions,

deletions, or insertions of one or more nucleotides. The substantially identical sequence often conforms to the $(G_aX_b)_cG_a$, $(GGA)_4$ (SEQ ID NO: 11) or $(GGA)_3GG$ (SEQ ID NO: 18) motifs described above. The term “substantially identical” refers to two or more nucleic acids sharing one or more identical nucleotide sequences. Included are nucleotide sequences that sometimes are 55%, 60%, 65%, 70%, 75%, 80%, or 85% identical to a native quadruplex-forming nucleotide sequence, and often are 90% or 95% identical to the native quadruplex-forming nucleotide sequence (each identity percentage can include a 1%, 2%, 3% or 4% variance). One test for determining whether two nucleic acids are substantially identical is to determine the percentage of identical nucleotide sequences shared between the nucleic acids.--

Please replace paragraph [0046], beginning on page 17 and bridging to page 18, with the following rewritten paragraph:

[0046] --A polymerase arrest assay is useful for determining whether transcription is modulated by a candidate molecule and/or a nucleic acid binding protein. Such an assay includes a template nucleic acid, which often comprises a quadruplex forming sequence, and a primer nucleic acid which hybridizes to the template nucleic acid 5' of the quadruplex-forming sequence. The primer is extended by a polymerase (*e.g.*, Taq polymerase), which advances from the primer along the template nucleic acid. In this assay, a quadruplex structure can block or arrest the advance of the enzyme, leading to shorter transcription fragments. Also, the arrest assay may be conducted at a variety of temperatures, including 45°C and 60°C, and at a variety of ion concentrations. An example of the Taq polymerase stop assay is described in Han, *et al.*, *Nucl. Acids Res.* 27:537-542 (1999), which is a modification of that used by Weitzmann, *et al.*, *J. Biol. Chem.* 271, 20958–20964 (1996). Briefly, a reaction mixture of template DNA (50 nM), Tris•HCl (50 mM), MgCl₂ (10 mM), DTT (0.5 mM), EDTA (0.1 mM), BSA (60 ng), and 5'-end-labeled quadruplex nucleic acid (~18 nM) is heated to 90°C for 5 minutes and allowed to cool to ambient temperature over 30 minutes. Taq Polymerase (1 µl) is added to the reaction mixture, and the reaction is maintained at a constant temperature for 30 minutes. Following the addition of 10 µl stop buffer (formamide (20 ml), 1 M NaOH (200 µl), 0.5 M EDTA (400 µl), and 10 mg bromophenol blue), the reactions are separated on a preparative gel (12%) and visualized on a phosphorimager. Adenine sequencing (indicated by “A” at the top of the gel) is performed

using double-stranded DNA Cycle Sequencing System from Life Technologies. The general sequence for the template strands is TCCAACATGTATAC (SEQ ID NO: 19)-INSERT-TTAGCGACACGCAATTGCTATAGTGAGTCGTATTA (SEQ ID NO: 20). Bands on the gel that exhibit slower mobility are indicative of quadruplex formation.--

Please replace paragraph [0047], beginning on page 18 and bridging to page 19, with the following rewritten paragraph:

[0047] --In another example of a polymerase arrest assay often utilized to determine the appropriate concentration of a test molecule used in the competition assays described herein, a 5'- fluorescent-labeled (FAM) primer (P45, 15 nM) is mixed with template DNA (15nM) in a Tris-HCL buffer (15 mM Tris, pH 7.5) containing 10mM MgCl₂, 0.1mM EDTA and 0.1mM mixed deoxynucleotide triphosphates (dNTP's). The FAM-P45 primer (5'- 6FAM-AGTCTGACTGACTGTACGTAGCTAATACGACTCACTATAGCAATT-3') (SEQ ID NO: 21) and the template DNA (5'-TCCAACATGTATACTGGGGAGGGTGGGGAGGGTG GGAAGGTTAGCGACACGCAATTGCTATAGTGAGTCGTATTAGCTACGTACAGTCAGTCAGACT-3') (SEQ ID NO: 22) are synthesized and HPLC purified by Applied Biosystems. The mixture is denatured at 95°C for 5 minutes and, after cooling down to room temperature, is incubated at 37°C for 15 minutes. After cooling down to room temperature, 1mM KCl₂ and the test compound (various concentrations) are added and the mixture incubated for 15 minutes at room temperature. The primer extension is performed by adding 10mM KCl and Taq DNA Polymerase (2.5 U/reaction, Promega) and incubating at 70°C for 30 minutes. The reaction is stopped by adding 1 µl of the reaction mixture to 10 µl Hi-Di Formamide mixed and 0.25 µl LIZ120 size standard. Hi-Di Formamide and LIZ120 size standard are purchased from Applied Biosystems. The partially extended quadruplex arrest product is between 61 or 62 bases long and the full-length extended product is 99 bases long. The products are separated and analyzed using capillary electrophoresis. Capillary electrophoresis is performed using an ABI PRISM 3100-Avant Genetic Analyzer.--

Please replace paragraph [0077], beginning on page 28 and bridging to page 29, with the following rewritten paragraph:

[0077] --For data presented in Figure 2, the DNA primer extension sequence FAM-P45 (5'-6FAM-AGT CTG ACT GAC TGT ACG TAG CTA ATA CGA CTC ACT ATA) (SEQ ID NO: 23), the Template sequence

(5'-TCCA ACTATCTATACT**TGGGGAGGGTGGGGAGGG**
TGGGGAAGGTTAGCGACACGCAATTGCTATAGTGAGTCGGTATTACTATCA-3'

(SEQ ID NO: 24), the portion in bold corresponds to the Myc27 second nucleic acid described hereafter) and the competition sequences (Myc27:

5'-TGGGGAGGGTGGGGAGGGTGGGGA AGG-3' (SEQ ID NO: 25), PDGFA-31:

5'-GGGGGGGCGGGGGCGGGGGCGGGGGAGGG GC-3' (SEQ ID NO: 26), HIF1A-31:

5'-GCGCGGGGAGGGGAGAGGGGGCGGGAGCG CG-3' (SEQ ID NO: 27)) were made

and HPLC purified by Qiagen. The duplex DNA, which was also used as a competition sequence, was synthesized using the single strand DNA

(5'-GCATCAGTCATCAGTCGTACTGCAT-3') (SEQ ID NO: 28) and its anti-sense

sequence which was made and HPLC purified by Qiagen. Plasmid DNA corresponded to

pSV-β-Galactosidase Vector, 6820bp and the 2.7 kilobase commercially available pUC18

also could be utilized. Hi-Di Formamide and LIZ120 size standard are commercially

available from Applied Biosystem. Taq DNA Polymerase is commercially available from

Promega. Capillary electrophoresis was performed on an ABI PRISM 3100-Avant Genetic Analyzer.--